Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 inhibitor, in moderate to severe plaque psoriasis: 2-year efficacy by prior biologic treatment in the phase 3 POETYK PSO program

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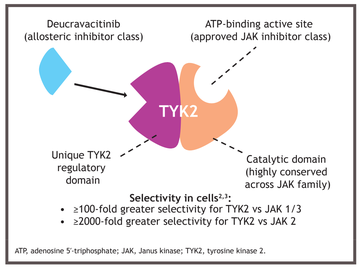
Introduction

- Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, is approved in the US and other countries for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy[1]
- Deucravacitinib has a unique mechanism of action distinct from Janus kinase (JAK) 1/2/3 inhibitors[2,3] (**Figure 1**)
  - Binds to the TYK2 regulatory domain and inhibits TYK2 via an allosteric mechanism[2]
  - Inhibits TYK2-mediated signaling of cytokines involved in psoriasis pathogenesis (eg, interleukin [IL]-23 and Type I interferons)[2]
- Deucravacitinib was significantly more efficacious than placebo or apremilast and was well tolerated in patients with moderate to severe plaque psoriasis in the 52-week, phase 3 POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) trials[4,5]

Figure 1. Mechanism of action of deucravacitinib



ATP, adenosine 5′-triphosphate; JAK, Janus kinase; TYK2, tyrosine kinase 2.

Objective

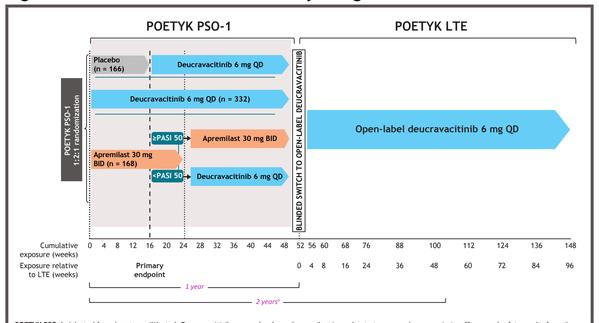
- The current analyses were performed to evaluate the effect of prior biologic treatment on long-term clinical efficacy in patients who received continuous deucravacitinib treatment in POETYK PSO-1 from Day 1 for up to 2 years in the POETYK long-term extension (LTE; NCT04036435) trial

Methods

Study designs

- POETYK PSO-1 was a 52-week, phase 3, double-blind trial that randomized patients with moderate to severe plaque psoriasis 1:2:1 to oral placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily
- At Week 52, all qualified patients who completed POETYK PSO-1 (or POETYK PSO-2) were eligible to enroll in the POETYK LTE trial and receive open-label deucravacitinib 6 mg once daily for up to 2 years (**Figure 2**)
- Key eligibility criteria included the following:
  - Age ≥18 years
  - Diagnosis of moderate to severe plaque psoriasis
    - Baseline Psoriasis Area and Severity Index (PASI) ≥12, static Physician's Global Assessment (sPGA) ≥3, and body surface area (BSA) involvement ≥10%

Figure 2. POETYK PSO-1 and LTE study designs



POETYK PSO-1: Adapted from Armstrong AW, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. *J Am Acad Dermatol*. 2023;88:29-39. https://www.jaad.org/action/showPdf?pii=S0190-9622%2822%2902256-3. This work is licensed under a Creative Commons Attribution License (CC BY-NC-ND 4.0). https://creativecommons.org/licenses/by-nc-nd/4.0/.

*Data reported through the 120-day LTE cutoff date of October 1, 2021.

BID, twice daily; LTE, long-term extension; PASI 50, ≥50% reduction from baseline in Psoriasis Area and Severity Index; QD, once daily.

Analysis population

- Patients who received continuous deucravacitinib from Day 1 (Week 0) in POETYK PSO-1 and subsequently entered the POETYK LTE were analyzed

Assessments and statistical analyses

- Efficacy, defined as ≥75% reduction from baseline in PASI (PASI 75), ≥90% reduction from baseline in PASI (PASI 90), and an sPGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (sPGA 0/1), was assessed in patients with up to 112 weeks of continuous deucravacitinib exposure stratified by prior biologic treatment in the following subgroups:
  - Biologic naive
  - Anti-tumor necrosis factor (TNF) experienced
  - Anti-IL-17/anti-IL-23 experienced
- Modified nonresponder imputation (mNRI)[6] was used to impute missing data
  - Multiple imputation was used for missing data, and patients who discontinued due to worsening of psoriasis were imputed as nonresponders
  - Only patients who discontinued or reached Week 112 by the data cutoff date (October 1, 2021) were included

Results

Baseline patient demographics and disease characteristics

- A total of 332 patients were randomized to deucravacitinib treatment in POETYK PSO-1
  - Biologic naive (n = 191 [57.5%])
  - Anti-TNF experienced (n = 52 [15.7%]): adalimumab (n = 35), certolizumab (n = 7), etanercept (n = 16), and infliximab (n = 3)
  - Anti-IL-17/anti-IL-23 experienced (n = 89 [26.8%]): bimekizumab (n = 2), briakinumab (n = 2), brodalumab (n = 19), guselkumab (n = 12), ixekizumab (n = 26), risankizumab (n = 1), secukinumab (n = 33), tildrakizumab (n = 1), and ustekinumab (n = 13)
- A total of 265 patients (79.8% of patients randomized at Day 1) received continuous deucravacitinib treatment from Day 1 in POETYK PSO-1 until Week 112 in the POETYK LTE (**Table 1**)
  - Biologic naive: n = 157 (59.2%)
  - Anti-TNF experienced: n = 36 (13.6%)
  - Anti-IL-17/anti-IL-23 experienced: n = 72 (27.2%)
- Baseline demographics and disease characteristics of patients who received continuous deucravacitinib treatment from Day 1 through Week 112 were consistent with the characteristics of the POETYK PSO-1 population[4]

Table 1. Baseline patient demographics and disease characteristics in POETYK PSO-1

Parameter	Patients randomized to deucravacitinib on Day 1 (N = 332)	Patients who were randomized to deucravacitinib and continued through Week 112 in the POETYK LTE (N = 265)
Age, mean (SD), y	45.9 (13.7)	46.0 (13.7)
Weight, mean (SD), kg	87.9 (21.8)	87.0 (22.2)
Female, n (%)	102 (30.7)	87 (32.8)
Race, n (%)		
White	267 (80.4)	211 (79.6)
Asian	59 (17.8)	51 (19.2)
Black or African American	2 (0.6)	1 (0.4)
Other	4 (1.2)	2 (0.8)
Age at disease onset, mean (SD), y	29.6 (15.1)	29.8 (15.1)
Disease duration, mean (SD), y	17.1 (12.4)	17.0 (12.2)
PASI score, mean (SD)	21.8 (8.6)	21.8 (8.3)
sPGA score, n (%)		
3 (moderate)	257 (77.4)	208 (78.5)
4 (severe)	75 (22.6)	57 (21.5)
BSA involvement, mean (SD), %	26.6 (15.9)	27.2 (15.6)

BSA, body surface area; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; SD, standard deviation; sPGA, static Physician's Global Assessment.

Efficacy

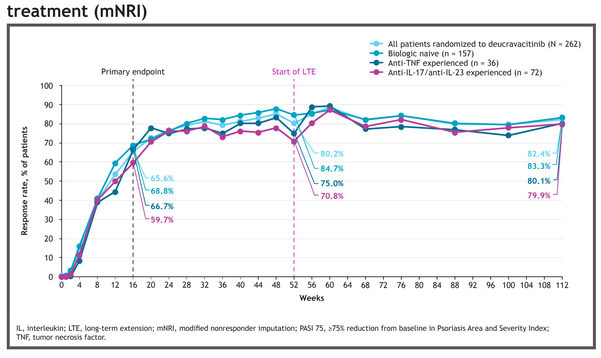
- High clinical responses were observed at Week 112 in each prior biologic treatment subgroup (**Table 2**; **Figures 3-5**)

Table 2. Week 112 clinical responses in each prior biologic treatment subgroup

Outcomes	Response rate, % of patients	Figure
PASI 75		3
Total	82.4	
Biologic naive	83.3	
Anti-TNF experienced	80.1	
Anti-IL-17 / anti-IL-23 / anti-IL-12/ anti-IL-23 experienced	79.9	
PASI 90		4
Total	55.2	
Biologic naive	54.3	
Anti-TNF experienced	55.9	
Anti-IL-17 / anti-IL-23 / anti-IL-12/ anti-IL-23 experienced	53.3	
sPGA 0/1		5
Total	66.5	
Biologic naive	67.1	
Anti-TNF experienced	67.1	
Anti-IL-17 / anti-IL-23 / anti-IL-12/ anti-IL-23 experienced	62.6	

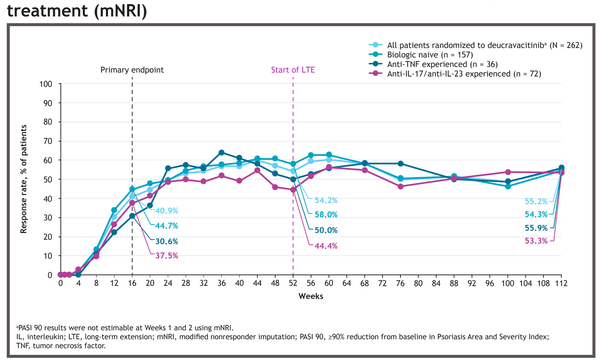
IL, interleukin; PASI 75/90, ≥75%/≥90% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline; TNF, tumor necrosis factor.

Figure 3. PASI 75 response rates through Week 112 in patients treated with continuous deucravacitinib and stratified by prior biologic treatment (mNRI)



IL, interleukin; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; TNF, tumor necrosis factor.

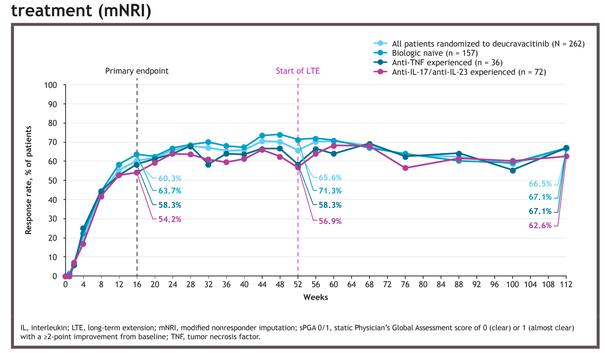
Figure 4. PASI 90 response rates through Week 112 in patients treated with continuous deucravacitinib and stratified by prior biologic treatment (mNRI)



[a]PASI 90 results were not estimable at Weeks 1 and 2 using mNRI.

IL, interleukin; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 90, ≥90% reduction from baseline in Psoriasis Area and Severity Index; TNF, tumor necrosis factor.

Figure 5. sPGA 0/1 response rates through Week 112 in patients treated with continuous deucravacitinib and stratified by prior biologic treatment (mNRI)



IL, interleukin; LTE, long-term extension; mNRI, modified nonresponder imputation; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline; TNF, tumor necrosis factor.

Conclusions

- Deucravacitinib maintained clinical efficacy well for over 2 years in patients who received continuous treatment regardless of prior exposure to different classes of biologic agents
  - PASI 75, PASI 90, and sPGA 0/1 responses were similar in patients who were biologic naive, anti-TNF experienced, or anti-IL-17/anti-IL-23 experienced as in the overall randomized deucravacitinib population
- These findings further support deucravacitinib, a once-daily oral drug, as an efficacious therapeutic option for patients with moderate to severe plaque psoriasis regardless of prior biologic treatment history

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